

## ABSTRACT

The present invention provides methods and compositions for regulating ubiquitination in a cell. In particular, the present invention provides purified polypeptides comprising an ubiquitination-regulating domain. The invention also provides methods of using such polypeptides for screening for agents, for producing antibodies, and for treatment of diseases, e.g., proliferative diseases, neurodegenerative diseases, autoimmune diseases, metabolic disease and developmental abnormalities. The invention further provides antibodies that bind an ubiquitination-regulating domain and agents and antibodies that regulate ubiquitination in cells, e.g., by modulating the interaction between a TSG101 protein and an MDM2 protein.